REMARKS

Claims 45-62 are pending. Favorable reconsideration is respectfully requested.

The objection to the claims is believed to be obviated by the amendment submitted above. Newly-added Claim 45 does not recite the non-elected subject matter (C)-(H). Accordingly, withdrawal of this objection is respectfully requested.

The rejection of the claims under 35 U.S.C. §101 is believed to be obviated by the amendment submitted above. Newly-added Claim 45 recites the term "isolated.". Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of the claims under 35 U.S.C. §112, second paragraph, is believed to be obviated by the amendments submitted above. The newly-added claims specify a standard against which the increase of the expression amount is determined. In addition, clerical errors have been corrected. Withdrawal of this ground of rejection is respectfully requested.

The rejection of the claims under 35 U.S.C. §112, first paragraph, is believed to be obviated by the amendment submitted above in part and is, in part, respectfully traversed.

The Examiner has stated that Claim 1, now embodied in Claim 45, is not limited to a modified bacterium with increased polypeptide expression by increasing a nucleic acid copy number. However, the increase of the expression amount by replacing the expression regulatory sequence is a well established technique in the art, as described on page 11, lines 17-25 of the present specification. This is demonstrated by the following publications, copies of which are submitted herewith for the Examiner's convenience:

(1) Journal of Biotechnology, 5 (1987) 237-253

(2) EP 0 593 792 A1.

In view of the fact that increasing the expression amount of a protein by replacing the expression regulatory sequence is a well established technique in the art, the scope of the amended claims is believed to be enabled by the present specification.

The Examiner has stated that the activity of the disclosed polypeptides is the export of amino acid. The newly-added claims recite excreting the L-amino acid.

The Examiner also stated that the present specification does not demonstrate increased yields of any other amino acids besides proline, lysine, and glutamate. The newly-added claims are directed to these amino acids.

Based on the foregoing, the claims are enabled. Accordingly withdrawal of this ground of rejection is respectfully requested.

The rejection of the claims under 35 U.S.C. §103(a) as being unpatentable over Blatter et al. (GenBank [sic, SWISS-PROT seems to be correct.] Accession Number P75693) in view of Vrljic et al. (Mol. Microbiol. 22:815-826), and U.S. Patent No. 6,040,160, is respectfully traversed.

The Examiner has taken the position that Blatter et al. teach that YAHN polypeptide is a transmembrane protein and that the YAHN polypeptide, based on sequence homology using the Pfam database, belongs to the LysE protein family. However, Blatter et al. provide information only on the homology. The reference fails to show whether the YAHN polypeptide is actually an L-amino acid-excreting protein or not. In fact, at the time the present application was filed, nothing was known about a gene participating in excretion of *E. coli*.

It is known that if genes are selected by homology search with respect to a known gene, some genes do not have the same function as that of the known gene. Moreover, it is known that even if a gene is classified in the same category as that of the gene participating

in excretion based on the homology, there are cases where substances to be excreted are quite different from one another, e.g., one is for excretion of an amino acid, and the other is for excretion of a substance other than an amino acid. Therefore, even if a homologue is obtained by homology search for a gene participating in an amino acid excretion system, it is not reasonably expected whether the homologue participates in the amino acid excretion system (in particular, excretion system of the intended amino acid) or not. In J. Mol. Microbiol: Biotechnol. 1999. 1(2): 327-336, a copy of which is submitted herewith, it is described that homology search of the LysE family is carried out, YahN has obtained only with a poor score (see pages 333-334). To obtain the object gene based on the homology of the poor score, inventive trial and error are needed. Therefore, it is not reasonably expected that the gene is a gene participating in amino acid excretion with a homology having such a low score.

Even if additional information is used, it is believed that the function of the gene cannot be reasonably expected based on only the sequence information. Three families constitute the LysE superfamily: the LysE family, the YahN (or RhtB) family, and the CadD family. Even in the CadD family among the superfamily, one participating in cadmium resistance and one suggested to be participating in a quaternary amine excretion system are known (see page 334 of the reference cited above). It is not reasonable to conclude that two genes are the same or similar function based on only the homology therebetween of this extent.

Vrljic et al. (Mol. Microbiol. 22:815-826) simply discloses overexpression of the lysE gene. U.S. Patent No. 6,040,160 simply suggests using a homologous gene. These references do not remedy the basic inadequacy of Blatter et al. to make the present invention obvious.

Based on the foregoing, Claims 45-62 are not obvious over the cited references. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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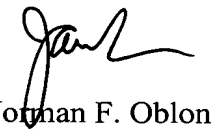

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IN THE CLAIMS

--Claims 1-44 (Cancelled)

Claims 45-62 (New).--